

Application Number: Pending

Docket: 7214.07

*Conclusion*

In view of the foregoing, Applicant submits that all pending claims are allowable. The Examiner is invited to telephone the undersigned attorney for Applicants in the event that such communication is deemed to expedite prosecution of this application.

Respectfully submitted,

DORSEY & WHITNEY LLP

Date: October 19, 2001

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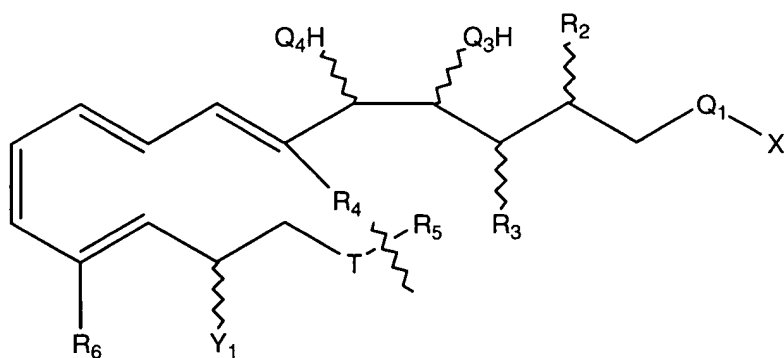
Telephone: (612) 340-8819

Facsimile: (612) 340-8856

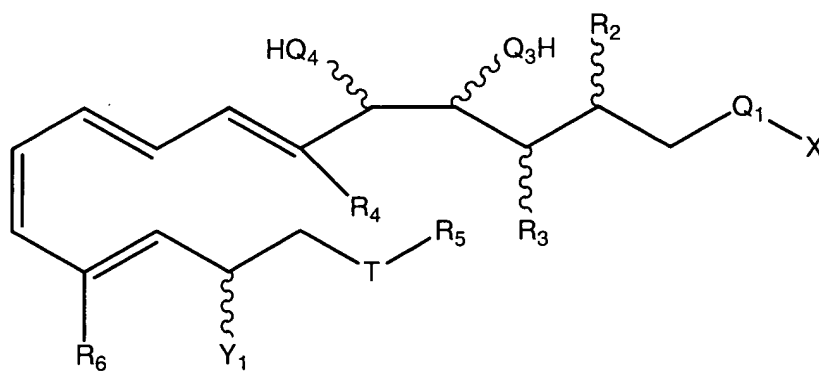
**MARKED-UP VERSION SHOWING CHANGES**

In the specification:

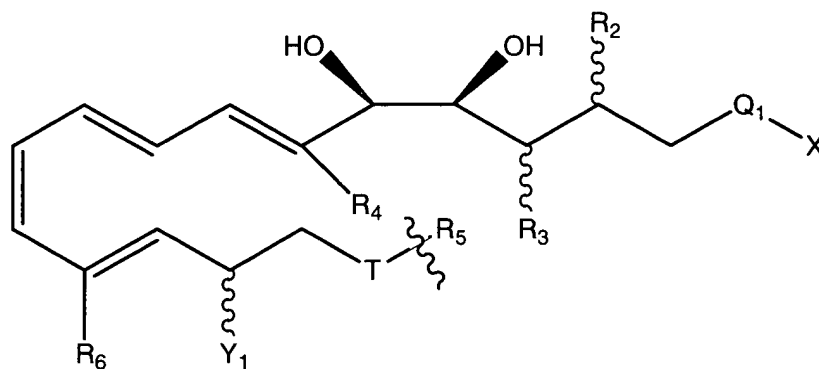
At page 11, lines 5 through 10, please delete



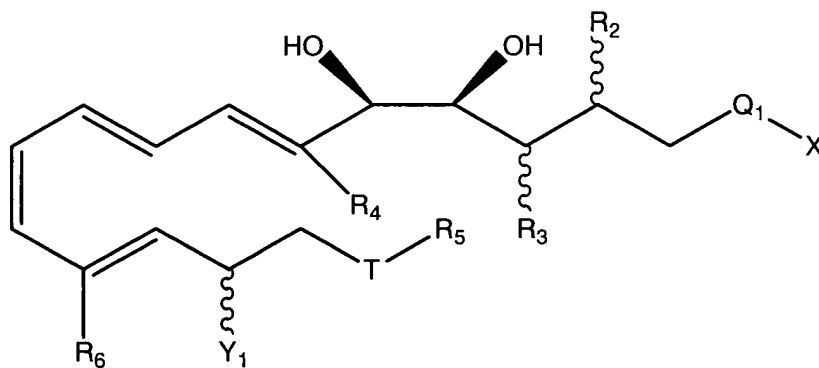
and insert therefore - -



At page 14, lines 1 through 7, please delete

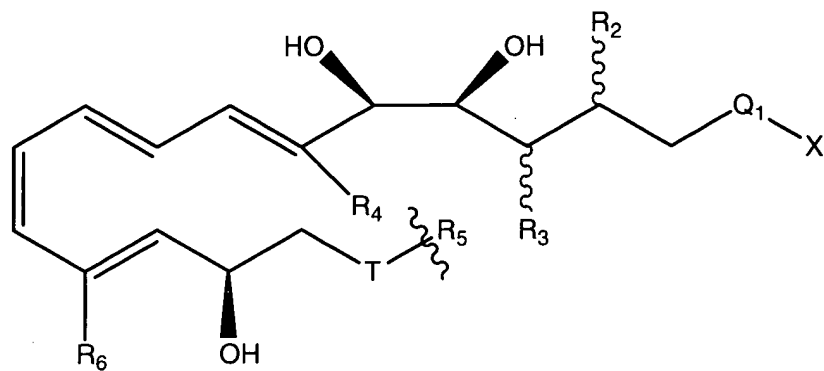


and insert therefore - -

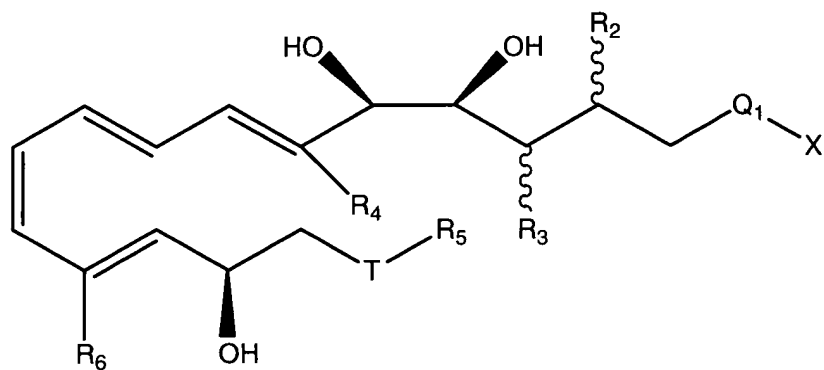


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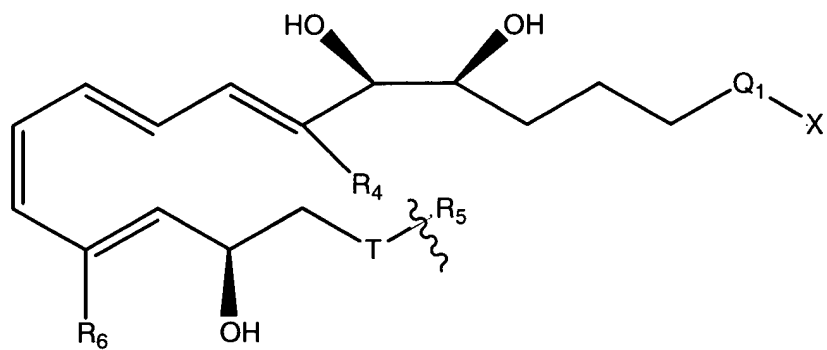
At page 17, lines 1 through 7, please delete



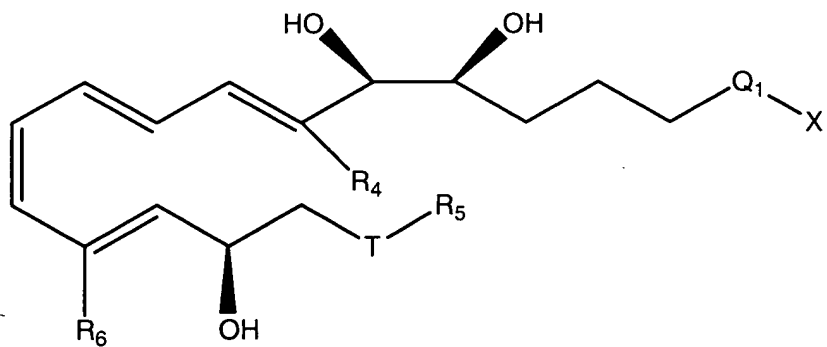
and insert therefore - -



At page 19, lines 21 through 30, please delete



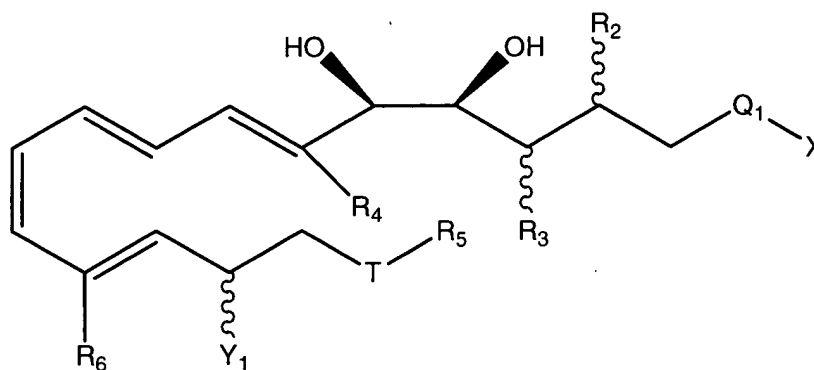
and insert therefore - -



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In the claims:

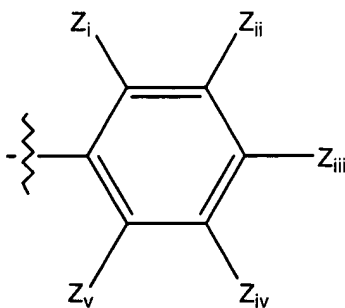
17. (New) A method for modulating a disease or condition associated with phospholipase D (PLD) initiated polymorphonuclear (PMN) inflammation in a subject, comprising administering to the subject an effective anti-inflammatory amount of a lipoxin analog having the formula



wherein X is R<sub>1</sub>, OR<sub>1</sub>, or SR<sub>1</sub>;

wherein R<sub>1</sub> is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbon atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein  $\text{Q}_1$  is  $\text{C}=\text{O}$ ,  $\text{SO}_2$  or  $\text{CN}$ , provided when  $\text{Q}_1$  is  $\text{CN}$ , then  $\text{X}$  is absent;

wherein  $\text{Q}_3$  and  $\text{Q}_4$  are each independently  $\text{O}$ ,  $\text{S}$  or  $\text{NH}$ ;

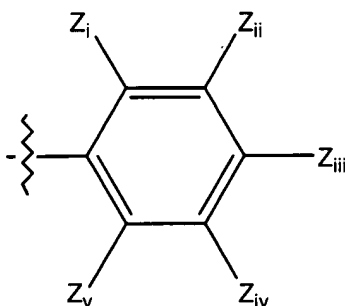
wherein one of  $\text{R}_2$  and  $\text{R}_3$  is a hydrogen atom and the other is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
- (e)  $\text{R}_a\text{Q}_2\text{R}_b$  wherein  $\text{Q}_2$  is  $-\text{O}-$  or  $-\text{S}-$ ; wherein  $\text{R}_a$  is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein  $\text{R}_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $\text{R}_b$  is 0, then  $\text{R}_b$  is a hydrogen atom;

wherein  $\text{R}_4$  is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $\text{R}_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

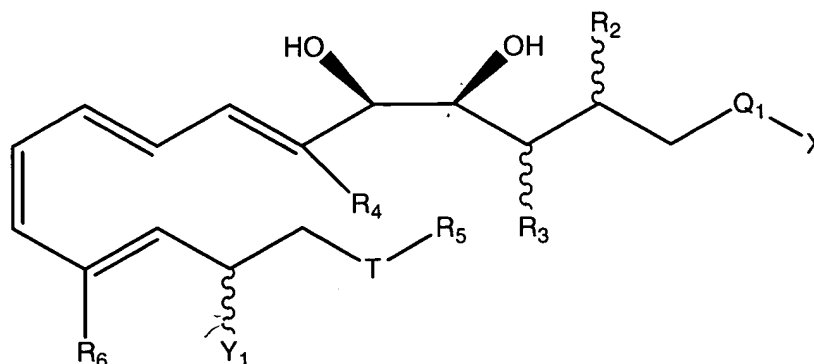
wherein  $\text{Y}_1$  is  $-\text{OH}$ , methyl,  $-\text{SH}$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $\text{CH}_a\text{Z}_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $\text{Z}$  is cyano, nitro or a halogen;

wherein  $\text{R}_6$  is

- (a) H;
- (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $\text{T}$  is O or S, and pharmaceutically acceptable salts thereof, such that a disease or condition associated with PLD initiated polymorphoneutrophil (PMN) inflammation in a subject is modulated.

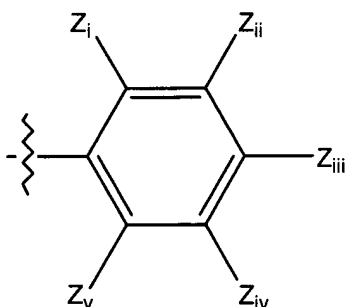
18. (New) The method of claim 17, wherein said method is performed *in vitro*.
19. (New) The method of claim 17, wherein said method is performed *in vivo*.
20. (New) A method for treating phospholipase D (PLD) initiated polymorphoneutrophil (PMN) inflammation in a subject, comprising administering to the subject an effective anti-inflammatory amount of a lipoxin analog having the formula



wherein X is R<sub>1</sub>, OR<sub>1</sub>, or SR<sub>1</sub>;

wherein R<sub>1</sub> is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbon atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein Z<sub>i</sub>, Z<sub>ii</sub>, Z<sub>iii</sub>, Z<sub>iv</sub> and Z<sub>v</sub> are each independently selected from -NO<sub>2</sub>, -CN, -C(=O)-R<sub>1</sub>, -SO<sub>3</sub>H, a hydrogen atom, halogen, methyl, -OR<sub>x</sub>, wherein R<sub>x</sub> is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q<sub>1</sub> is (C=O), SO<sub>2</sub> or (CN), provided when Q<sub>1</sub> is CN, then X is absent;

wherein Q<sub>3</sub> and Q<sub>4</sub> are each independently O, S or NH;

wherein one of R<sub>2</sub> and R<sub>3</sub> is a hydrogen atom and the other is

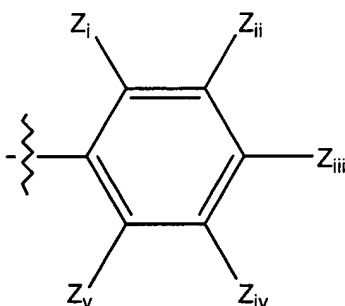
- (a) H;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

- (e)  $R_a Q_2 R_b$  wherein  $Q_2$  is  $-O-$  or  $-S-$ ; wherein  $R_a$  is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein  $R_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $R_b$  is 0, then  $R_b$  is a hydrogen atom;

wherein  $R_4$  is

- (a) H;  
 (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $R_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-NO_2$ ,  $-CN$ ,  $-C(=O)-R_1$ ,  $-SO_3H$ , a hydrogen atom, halogen, methyl,  $-OR_x$ , wherein  $R_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

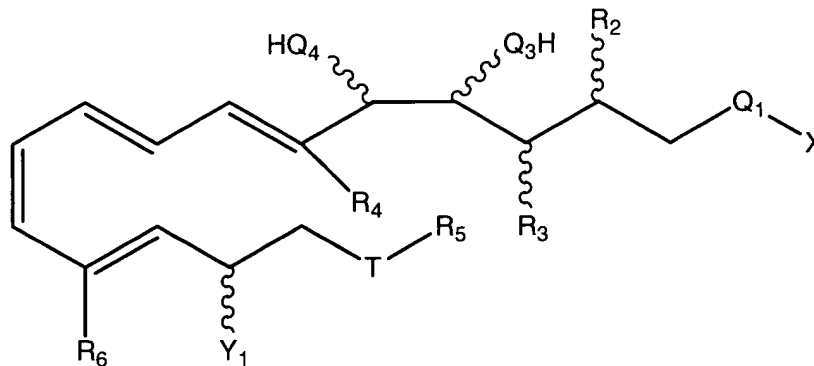
wherein  $Y_1$  is  $-OH$ , methyl,  $-SH$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $CH_a Z_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $Z$  is cyano, nitro or a halogen;

wherein  $R_6$  is

- (a) H;  
 (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $T$  is O or S, and pharmaceutically acceptable salts thereof, such that PLD initiated polymorphoneutrophil (PMN) inflammation is treated in a subject.

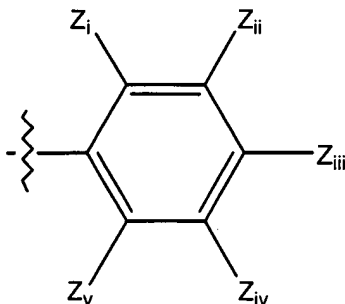
21. (New) The method of claim 20, wherein said method is performed *in vitro*.
22. (New) The method of claim 20, wherein said method is performed *in vivo*.
23. (New) A method for modulating a disease or condition associated with phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising administering to the subject an effective anti-PLD amount of a lipoxin analog having the formula



wherein X is R<sub>1</sub>, OR<sub>1</sub>, or SR<sub>1</sub>;

wherein R<sub>1</sub> is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbon atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein  $\text{Q}_1$  is  $(\text{C}=\text{O})$ ,  $\text{SO}_2$  or  $(\text{CN})$ , provided when  $\text{Q}_1$  is  $\text{CN}$ , then  $\text{X}$  is absent;

wherein  $\text{Q}_3$  and  $\text{Q}_4$  are each independently  $\text{O}$ ,  $\text{S}$  or  $\text{NH}$ ;

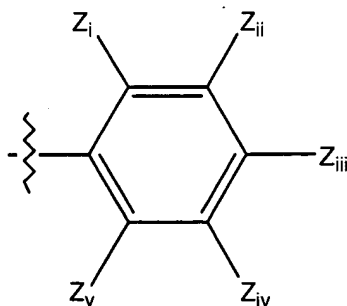
wherein one of  $\text{R}_2$  and  $\text{R}_3$  is a hydrogen atom and the other is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
- (e)  $\text{R}_a\text{Q}_2\text{R}_b$  wherein  $\text{Q}_2$  is  $-\text{O}-$  or  $-\text{S}-$ ; wherein  $\text{R}_a$  is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein  $\text{R}_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $\text{R}_b$  is 0, then  $\text{R}_b$  is a hydrogen atom;

wherein  $\text{R}_4$  is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $\text{R}_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein  $\text{Y}_1$  is  $-\text{OH}$ , methyl,  $-\text{SH}$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $\text{CH}_a\text{Z}_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $\text{Z}$  is cyano, nitro or a halogen;

wherein  $\text{R}_6$  is

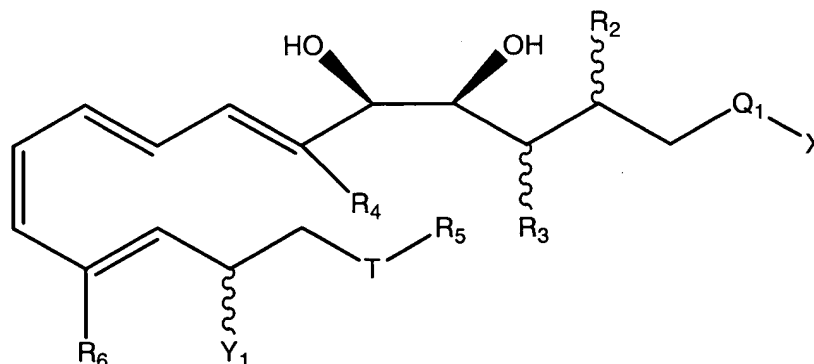
- (a) H;
- (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $\text{T}$  is O or S, and pharmaceutically acceptable salts thereof, such that a disease or condition associated with PLD initiated superoxide generation or degranulation activity in a subject is modulated.

24. (New) The method of claim 23, wherein said method is performed *in vitro*.

25. (New) The method of claim 23, wherein said method is performed *in vivo*.

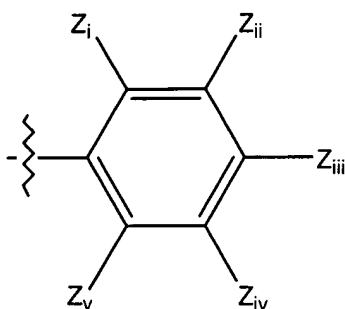
26. (New) A method for treating phospholipase D (PLD) initiated superoxide generation or degranulation in a subject, comprising administering to the subject an effective anti-PLD amount of a lipoxin analog having the formula



wherein X is R<sub>1</sub>, OR<sub>1</sub>, or SR<sub>1</sub>;

wherein R<sub>1</sub> is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbon atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein Z<sub>i</sub>, Z<sub>ii</sub>, Z<sub>iii</sub>, Z<sub>iv</sub> and Z<sub>v</sub> are each independently selected from -NO<sub>2</sub>, -CN, -C(=O)-R<sub>1</sub>, -SO<sub>3</sub>H, a hydrogen atom, halogen, methyl, -OR<sub>x</sub>, wherein R<sub>x</sub> is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q<sub>1</sub> is (C=O), SO<sub>2</sub> or (CN), provided when Q<sub>1</sub> is CN, then X is absent;

wherein Q<sub>3</sub> and Q<sub>4</sub> are each independently O, S or NH;

wherein one of R<sub>2</sub> and R<sub>3</sub> is a hydrogen atom and the other is

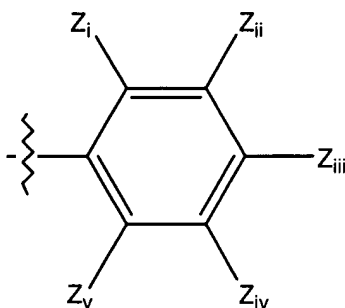
- (a) H;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

- (e)  $R_a Q_2 R_b$  wherein  $Q_2$  is  $-O-$  or  $-S-$ ; wherein  $R_a$  is alkylene of 0 to 6 carbon atoms, inclusive, which may be straight chain or branched and wherein  $R_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $R_b$  is 0, then  $R_b$  is a hydrogen atom;

wherein  $R_4$  is

- (a) H;  
 (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $R_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-NO_2$ ,  $-CN$ ,  $-C(=O)-R_1$ ,  $-SO_3H$ , a hydrogen atom, halogen, methyl,  $-OR_x$ , wherein  $R_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

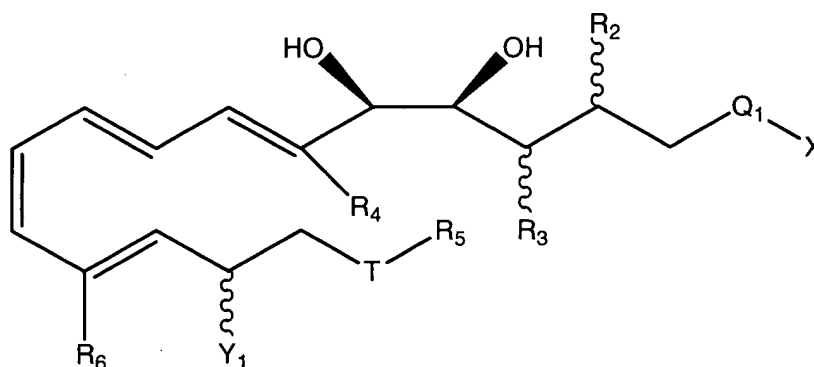
wherein  $Y_1$  is  $-OH$ , methyl,  $-SH$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $CH_a Z_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $Z$  is cyano, nitro or a halogen;

wherein  $R_6$  is

- (a) H;  
 (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $T$  is O or S, and pharmaceutically acceptable salts thereof, such that PLD initiated superoxide generation or granulation is treated in a subject.

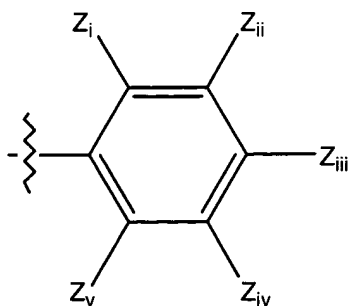
27. (New) The method of claim 26, wherein said method is performed *in vitro*.
28. (New) The method of claim 26, wherein said method is performed *in vivo*.
29. (New) A packaged pharmaceutical composition for treating a disease or condition associated with phospholipase D (PLD) initiated activity in a subject, comprising:  
a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R<sub>1</sub>, OR<sub>1</sub>, or SR<sub>1</sub>;

wherein R<sub>1</sub> is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein  $\text{Q}_1$  is  $\text{C}=\text{O}$ ,  $\text{SO}_2$  or  $\text{CN}$ , provided when  $\text{Q}_1$  is  $\text{CN}$ , then  $\text{X}$  is absent;

wherein  $\text{Q}_3$  and  $\text{Q}_4$  are each independently  $\text{O}$ ,  $\text{S}$  or  $\text{NH}$ ;

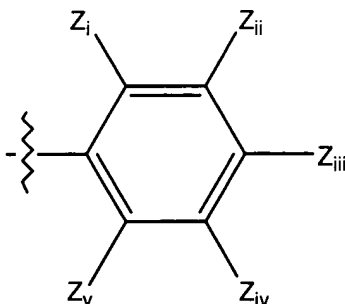
wherein one of  $\text{R}_2$  and  $\text{R}_3$  is a hydrogen atom and the other is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
- (e)  $\text{R}_a\text{Q}_2\text{R}_b$  wherein  $\text{Q}_2$  is  $-\text{O}-$  or  $-\text{S}-$ ; wherein  $\text{R}_a$  is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein  $\text{R}_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $\text{R}_b$  is 0, then  $\text{R}_b$  is a hydrogen atom;

wherein  $\text{R}_4$  is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $\text{R}_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein  $\text{Y}_1$  is  $-\text{OH}$ , methyl,  $-\text{SH}$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $\text{CH}_a\text{Z}_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $\text{Z}$  is cyano, nitro or a halogen;

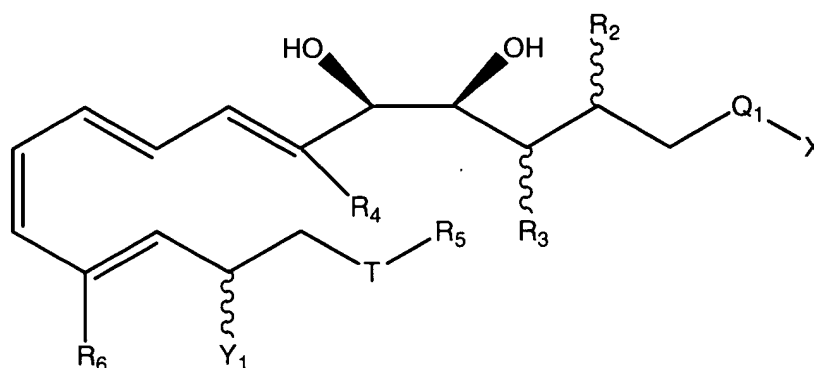
wherein  $\text{R}_6$  is

- (a) H;
- (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $\text{T}$  is O or S, and pharmaceutically acceptable salts thereof; and instructions for using said lipoxin compound for treating a disease or condition associated with PLD initiated activity in the subject.

30. (New) A packaged pharmaceutical composition for treating phospholipase D initiated activity in a subject, comprising:

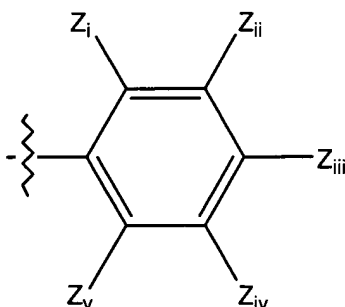
a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R<sub>1</sub>, OR<sub>1</sub>, or SR<sub>1</sub>;

wherein R<sub>1</sub> is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein Z<sub>i</sub>, Z<sub>ii</sub>, Z<sub>iii</sub>, Z<sub>iv</sub> and Z<sub>v</sub> are each independently selected from -NO<sub>2</sub>, -CN, -C(=O)-R<sub>1</sub>, -SO<sub>3</sub>H, a hydrogen atom, halogen, methyl, -OR<sub>x</sub>, wherein R<sub>x</sub> is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q<sub>1</sub> is (C=O), SO<sub>2</sub> or (CN), provided when Q<sub>1</sub> is CN, then X is absent;

wherein Q<sub>3</sub> and Q<sub>4</sub> are each independently O, S or NH;

wherein one of R<sub>2</sub> and R<sub>3</sub> is a hydrogen atom and the other is

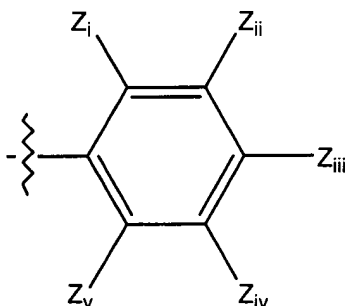
- (a) H;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

- (e)  $R_a Q_2 R_b$  wherein  $Q_2$  is  $-O-$  or  $-S-$ ; wherein  $R_a$  is alkylene of 0 to 6 carbon atoms, inclusive, which may be straight chain or branched and wherein  $R_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $R_b$  is 0, then  $R_b$  is a hydrogen atom;

wherein  $R_4$  is

- (a) H;  
 (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $R_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-NO_2$ ,  $-CN$ ,  $-C(=O)-R_1$ ,  $-SO_3H$ , a hydrogen atom, halogen, methyl,  $-OR_x$ , wherein  $R_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein  $Y_1$  is  $-OH$ , methyl,  $-SH$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $CH_a Z_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $Z$  is cyano, nitro or a halogen;

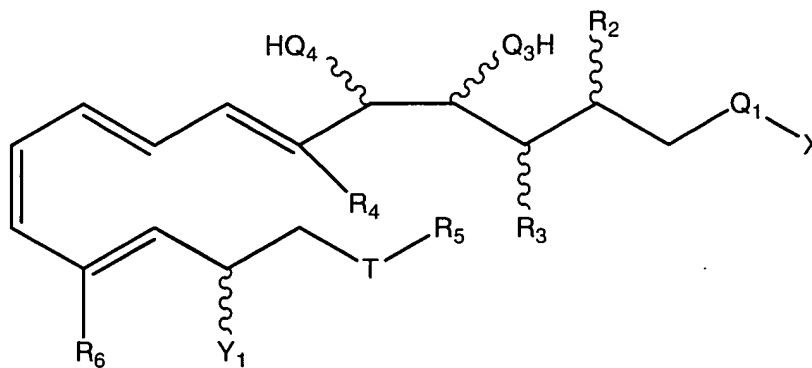
wherein  $R_6$  is

- (a) H;  
 (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $T$  is O or S, and pharmaceutically acceptable salts thereof; and instructions for using said lipoxin compound for treating PLD initiated activity in the subject.

31. (New) A packaged pharmaceutical composition for treating a disease or condition associated with phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising:

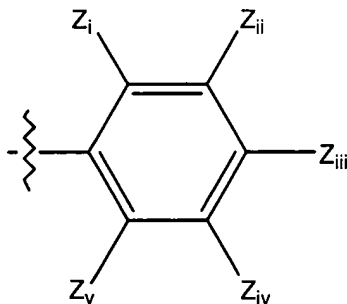
a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is  $R_1$ ,  $OR_1$ , or  $SR_1$ ;

wherein  $R_1$  is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbon atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein  $\text{Q}_1$  is  $(\text{C}=\text{O})$ ,  $\text{SO}_2$  or  $(\text{CN})$ , provided when  $\text{Q}_1$  is  $(\text{CN})$ , then  $\text{X}$  is absent;

wherein  $\text{Q}_3$  and  $\text{Q}_4$  are each independently  $\text{O}$ ,  $\text{S}$  or  $\text{NH}$ ;

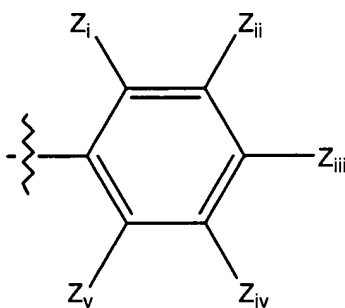
wherein one of  $\text{R}_2$  and  $\text{R}_3$  is a hydrogen atom and the other is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or
- (e)  $\text{R}_a\text{Q}_2\text{R}_b$  wherein  $\text{Q}_2$  is  $-\text{O}-$  or  $-\text{S}-$ ; wherein  $\text{R}_a$  is alkylene of 0 to 6 carbons atoms, inclusive, which may be straight chain or branched and wherein  $\text{R}_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $\text{R}_b$  is 0, then  $\text{R}_b$  is a hydrogen atom;

wherein  $\text{R}_4$  is

- (a)  $\text{H}$ ;
- (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $\text{R}_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-\text{NO}_2$ ,  $-\text{CN}$ ,  $-\text{C}(=\text{O})-\text{R}_1$ ,  $-\text{SO}_3\text{H}$ , a hydrogen atom, halogen, methyl,  $-\text{OR}_x$ , wherein  $\text{R}_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

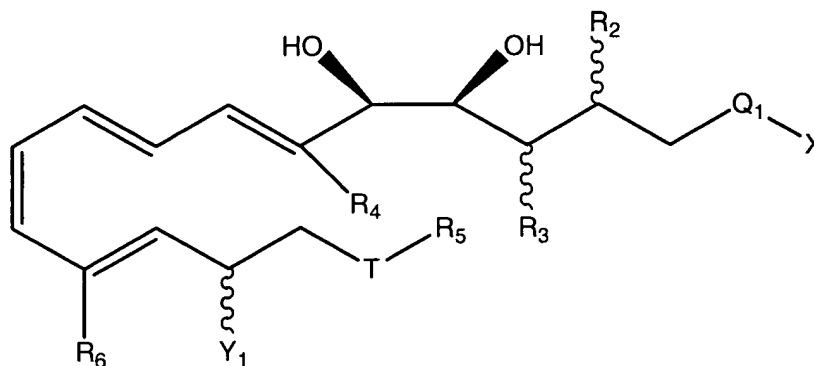
wherein  $\text{Y}_1$  is  $-\text{OH}$ , methyl,  $-\text{SH}$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $\text{CH}_a\text{Z}_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $\text{Z}$  is cyano, nitro or a halogen;

wherein  $\text{R}_6$  is

- (a) H;
- (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $\text{T}$  is O or S, and pharmaceutically acceptable salts thereof; and instructions for using said lipoxin compound for treating a disease or condition associated with PLD initiated superoxide generation or degranulation activity in the subject.

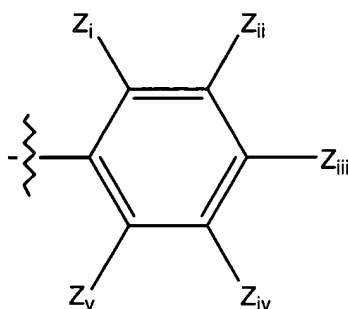
32. (New) A packaged pharmaceutical composition for treating phospholipase D (PLD) initiated superoxide generation or degranulation activity in a subject, comprising:  
a container holding a therapeutically effective amount of at least one lipoxin compound having the formula



wherein X is R<sub>1</sub>, OR<sub>1</sub>, or SR<sub>1</sub>;

wherein R<sub>1</sub> is

- (i) a hydrogen atom;
- (ii) an alkyl of 1 to 8 carbons atoms, inclusive, which may be straight chain or branched;
- (iii) a cycloalkyl of 3 to 10 carbon atoms;
- (iv) an aralkyl of 7 to 12 carbon atoms;
- (v) phenyl;
- (vi) substituted phenyl



wherein Z<sub>i</sub>, Z<sub>ii</sub>, Z<sub>iii</sub>, Z<sub>iv</sub> and Z<sub>v</sub> are each independently selected from -NO<sub>2</sub>, -CN, -C(=O)-R<sub>1</sub>, -SO<sub>3</sub>H, a hydrogen atom, halogen, methyl, -OR<sub>x</sub>, wherein R<sub>x</sub> is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl;

- (vii) a detectable label molecule; or
- (viii) a straight or branched chain alkenyl of 2 to 8 carbon atoms, inclusive;

wherein Q<sub>1</sub> is (C=O), SO<sub>2</sub> or (CN), provided when Q<sub>1</sub> is CN, then X is absent;

wherein Q<sub>3</sub> and Q<sub>4</sub> are each independently O, S or NH;

wherein one of R<sub>2</sub> and R<sub>3</sub> is a hydrogen atom and the other is

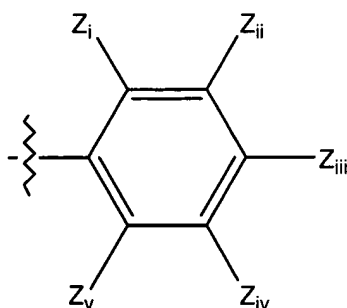
- (a) H;
- (b) an alkyl of 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched;
- (c) a cycloalkyl of 3 to 6 carbon atoms, inclusive;
- (d) an alkenyl of 2 to 8 carbon atoms, inclusive, which may be straight chain or branched; or

- (e)  $R_a Q_2 R_b$  wherein  $Q_2$  is  $-O-$  or  $-S-$ ; wherein  $R_a$  is alkylene of 0 to 6 carbon atoms, inclusive, which may be straight chain or branched and wherein  $R_b$  is alkyl of 0 to 8 carbon atoms, inclusive, which may be straight chain or branched, provided when  $R_b$  is 0, then  $R_b$  is a hydrogen atom;

wherein  $R_4$  is

- (a) H;  
 (b) an alkyl of 1 to 6 carbon atoms, inclusive, which may be a straight chain or branched;

wherein  $R_5$  is



wherein  $Z_i$ ,  $Z_{ii}$ ,  $Z_{iii}$ ,  $Z_{iv}$  and  $Z_v$  are each independently selected from  $-NO_2$ ,  $-CN$ ,  $-C(=O)-R_1$ ,  $-SO_3H$ , a hydrogen atom, halogen, methyl,  $-OR_x$ , wherein  $R_x$  is 1 to 8 carbon atoms, inclusive, which may be a straight chain or branched, and hydroxyl or a substituted or unsubstituted, branched or unbranched alkyl group;

wherein  $Y_1$  is  $-OH$ , methyl,  $-SH$ , an alkyl of 2 to 4 carbon atoms, inclusive, straight chain or branched, an alkoxy of 1 to 4 carbon atoms, inclusive, or  $CH_a Z_b$  where  $a+b=3$ ,  $a=0$  to 3,  $b=0$  to 3 and  $Z$  is cyano, nitro or a halogen;

wherein  $R_6$  is

- (a) H;  
 (b) an alkyl from 1 to 4 carbon atoms, inclusive, straight chain or branched;

wherein  $T$  is O or S, and pharmaceutically acceptable salts thereof; and

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instructions for using said lipoxin compound for treating PLD initiated superoxide generation or degranulation activity in the subject.

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